Remarks

Claims 1-3, 5-11, and 37 are pending; claims 1, 10, and 11 is amended herein. Claim 37 stands withdrawn from consideration.

The amendments to the claims are supported throughout the originally filed specification and claims. Amended claim 1 is supported, e.g., by originally filed claim 1, Table 21, SEQ ID NO:162, SEQ ID NO:150, and SEQ ID NOS: 186, 197, 244, 271, and 287, and at page 31, lines 5-14 and 21-25.

Residues 3200-3355 are one 156-amino acid repeat unit in SEQ ID NO:162 that is identical to SEQ ID NO:150 over the first 153 of the 156 amino acids. Two of the last 3 residues of SEQ ID NO:150 differ from the last three residues of the segment 3200-3355 of SEQ ID NO:162. SEQ ID NO:150 was expressed by recombinant DNA means as is reported in the specification to characterize a CA125 repeat unit, and two of the last three residues were different from the corresponding residues in SEQ ID NO:162 because there was a restriction enzyme splice site in the nucleic acid expression vector used to express the segment, and in designing the insertion sequence to fit this splice site, those two residues of the encoded protein became altered. Upon close inspection of the sequences disclosed in the specification, it would be clear to one of skill in the art that SEQ ID NO:150 as previously elected in the election of species requirement, corresponds to residues 3200-3355 of the full-length CA125 of SEQ ID NO:162 and consists of, in order, the exon-encoded multiple repeat unit segments of SEQ ID NOS: 186, 197, 244, 271, and 287, as recited in originally filed claim 1.

Amended claims 10 and 11 are supported by originally filed claims 10, 11, and 1.

The Rejection of the Claims under 35 U.S.C. § 112, First Paragraph

Claims 1-3 and 5-11 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification allegedly does not contain a written description of the invention. This rejection is respectfully traversed.

In section 6 of the Office Action, the basis of the written description rejection appears to be the use of the word "purified" in the preamble of claim 1. Claim 1 has been amended to recite "An isolated recombinant CA125 molecule." The amendment to the preamble of claim 1 is supported throughout the specification. For instance, the

specification discloses the cloning and sequencing of the complete genomic and cDNA genes encoding CA125. At page 31, lines 21-25, the specification discloses " With the availability of recombinant CA125, especially domains which encompass epitope binding sites for known murine antibodies and domains directly anchoring CA125 to the tumor cell, it will be feasible to more directly stimulate patients' immune systems to CA125 and as a result, extend the life of ovarian carcinoma patients as demonstrated by Wagner et al." The paragraph at page 31, lines 5-14 discusses advantages and uses of the CA125 recombinant products, and states: "Recombinant CA125 containing epitope binding sites could fulfill this need for standardization."

These passages provide express support for "An isolated recombinant CA125 molecule, as well as inherent and implicit support.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 'Written Description' Requirement (Fed. Register Vol. 66, No. 4, pp. 1099-1111, at p. 1105) state "there is no *in haec verba* requirement" to satisfy the written description requirement and newly added claim limitations can be "supported in the specification through express, implicit, or inherent disclosure." The Board of Patent Appeals and Interferences in *Ex parte Parks*, 30 U.S.P.Q.2d 1234 (Board of Patent Appeals and Interferences 1994) stated:

> Adequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention. . . . Rather, it is sufficient if the originally filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed. (Emphasis added.)

There can be no doubt at all that the concept of an isolated recombinant CA125 molecule is conveyed to one of ordinary skill in the art by the specification.

In section 7, claims 1-3 and 5-11 were rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description on the basis that the specification does not support variants of CA125 inclusive of combinations of the recited segments of the amino terminal domain and carboxy terminal domain in an order different from the order they are found in SEQ ID NO:299 and SEQ ID NO:300. Claim 1 is amended to

recite that the fragments previously recited are in order, and Applicants believe this obviates this basis for the rejection.

In section 8, claims 1-3 and 5-11 were rejected under the written description requirement on the basis that the claims do not limit the identity, number, or order of the multiple repeat sequences. At page 12, the Examiner stated that the specification does not provide the complete structure of a CA125 molecule comprising a multiple repeat domain comprising SEQ ID NO:150, nor does the specification provide any partial structure of such CA125 molecule, nor any physical or chemical characteristics of said CA125 molecule, nor any functional characteristics coupled with a known or disclosed correlation between structure and function.

Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, and functional characteristics alone or coupled with a known or disclosed correlation between structure and function. (*Guidelines for Examination of Patent Aplications Under the 35 U.S.C. 112, Paragraph 1, "Written Description" Requirement*, Fed. Reg. Vol. 66, No. 4, 2001, pages 1099-1111, at 1106.) The present claims and specification meet all of these factors.

The level of skill in the medical and biotechnology arts is high. The typical art worker has a Ph.D. and even some postdoctoral experience.

Applicant has disclosed not just a partial structure, but a complete structure of a recombinant CA125 molecule recited in the claims. Table 21 with SEQ ID NO:162 discloses the complete sequence of the CA125 protein encoded by the complete cDNA. Claim 1 has been amended to recite an isolated recombinant CA125 molecule comprising . . . (b) a multiple repeat domain comprising residues 3200 to 3355 of SEQ ID NO: 162. The specification discloses the complete structure of an isolated recombinant CA125 molecule comprising a multiple repeat domain comprising residues 3200 to 3355 of SEQ ID NO: 162. Residues 3200 to 3355 are one multiple repeat domain containing the exon-encoded segments recited in the originally filed claim 1 of SEQ ID NOS: 186, 197, 244, 271, and 287.

The physical and/or chemical properties of CA125 are provided in the form of a complete structure of CA125. Physical, chemical, and biological properties derived from the structure are also disclosed. For instance, N-glycosylation and O-glycosylation sites in a repeat unit are shown in FIG. 5 and described in page 9, lines 18-20. At page 21, line 55 to page 22, line 6, and page 9, lines 9-24, the specification discloses that cleavage at amino acids 76 or 68 of the repeat unit of SEQ ID NO:150 with Asp-N or Lys-C protease eliminates recognition of the peptide by the M11 antibody. (Residues 3200-3355 of SEQ ID NO:162, recited in the claims, are identical to SEQ ID NO:150 over the first 153 residues and the 156th residue of the 156-amino-acid SEQ ID NO:150.) The specification discloses in paragraph 101 that cysteines #59 and #79 of SEQ ID NO:150 are totally conserved in the multiple repeat units. Page 22, lines 23-26, also discloses that methionine #24 in SEQ ID NO:150 is also totally conserved in the multiple repeat units and that this accounts for cyanogen bromide digestion of CA125 resulting in a 40 kDa glycoprotein that is identified with OC125 and M11 antibodies. The specification concludes that from these data, it seems likely that the epitope binding residues in the cysteine loop region containing a possible disulfide bridge between cysteines #59-79 of the repeat unit (page 22, lines 4-5).

The specification discloses further that each multiple repeat unit is comprised of [segments encoded by] 5 exons whose sequences are provided (page 22, lines 8-23, and originally filed claim 1). It discloses that amino acids 1-42 of a multiple repeat are any of SEQ ID NOS:164-194, amino acids 43-65 are any of SEQ ID NOS:195-221, amino acids 66-123 are any of SEQ ID NOS:222-249, amino acids 124-135 are any of SEQ ID NOS:250-277, and amino acids 136-156 are any of SEQ ID NOS:278-298.

The specification discloses that because of the unusual length of CA125 and the homology between multiple repeat units, some of the multiple repeat units may have been incorrectly placed in SEQ ID NO:162, and some repeat units may not as yet be identified (page 23, lines 25-27). Because of this, it is not appropriate to limit the claims to a CA125 molecule having a single order and number of multiple repeat units in the multiple repeat domain.

The specification discloses the complete structure of a CA125 molecule as recited in the claims, and numerous physical, chemical, and biological characteristics of the

molecule, as well as the relationships of the characteristics to structure. All of the factors to be considered in determining whether there is sufficient evidence of possession listed in the *Guidelines for Examination of Patent Aplications Under the 35 U.S.C. 112, Paragraph 1, "Written Description" Requirement*, are satisfied by the present application. Because of the size and complexity of the CA125 molecule and in particular the multiple repeat domain, which was unknown prior to Applicants' invention and discovery, it is necessary for the claims not to be limited to a single order and number of multiple repeat units in the multiple repeat domain. Accordingly, Applicants respectfully submit that the application clearly satisfies the written description requirement for the present claims, reciting an isolated recombinant CA125 comprising . . .(b) a multiple repeat domain comprising residues 3200 to 3355 of SEQ ID NO: 162 . . . .

In section 9, claims 1-3 and 5-11 are rejected under 35 U.S.C. § 112, first paragraph as lacking an adequate written description on the basis that the specification does not provide a description of a carboxy terminal domain comprising a transmembrane anchor with a short cytoplasmic domain. Claim 1 has been amended to delete the language of a transmembrane anchor with a short cytoplasmic domain. Applicants believe this obviates this basis for the rejection.

Conclusion

Applicants respectfully submit that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (651-207-8270) to facilitate prosecution of this application.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient first class postage, in an envelope addressed to: Mail Stop Amendement, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 22 day of December 2006.

Hugh McTavish
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